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BOX PCT # 3

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: T. Saito Attorney Docket No: NAI118755  
Application No: 10/070,157 International App. No. PCT/JP00/06045  
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Title: METHOD OF PERFORATING MEMBRANE AND APPARATUS THEREFOR

**PRELIMINARY AMENDMENT**

Seattle, Washington 98101

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TO THE COMMISSIONER FOR PATENTS:

Please replace the claims 1-31 with claims 32-97, as follows:

32. A method of perforating a membrane comprising:

bringing a membrane-denaturing substance into contact with or close proximity to at least a site of said membrane, said substance inducing a membrane-denaturing reaction by a stimulus; providing said stimulus to said substance so as to denature said membrane; and perforating said membrane with a membrane-destroying member; wherein said stimulus is carried through said membrane-destroying member.

33. The method according to claim 32, wherein said membrane is a cell membrane, a cell wall, a biomembrane, or an artificial membrane.

34. The method according to claim 32, wherein said stimulus is selected from the group comprising electromagnetic waves including light, particle rays including radiation, heat, cooling, electricity, magnetism, oscillations including ultrasonic waves, physical contact, chemical substances, living beings including cells, viruses, and any combinations thereof.

35. The method according to claim 34, wherein said stimulus is light and said substance is a photosensitizer.

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36. The method according to claim 34, wherein said stimulus is light and said substance is a photocatalyst.

37. The method according to claim 32, wherein said membrane destroying member constitutes a supporting member for supporting the membrane-denaturing substance and a stimulus carrying member for carrying the stimulus.

38. The method according to claim 32, wherein said member is a capillary.

39. The method according to claim 37, wherein said member is a capillary.

40. The method according to claim 38, wherein said stimulus is light, said light transmits through the side wall of said capillary as a light guide, and said light is applied to said membrane-denaturing substance from the tip of said capillary.

41. The method according to claim 39, wherein said stimulus is light, said light transmits through the side wall of said capillary as a light guide, and said light is applied to said membrane-denaturing substance from the tip of said capillary.

42. The method according to claim 32, wherein said member is an intracellular sensor.

43. The method according to claim 37, wherein said member is an intracellular sensor.

44. A method of perforating a membrane comprising:  
bringing a membrane-denaturing substance into contact with or close proximity to at least a site of said membrane, said substance inducing a membrane-denaturing reaction by a stimulus;  
said bringing done by a supporting member for supporting said substance; and  
providing said stimulus to said substance so as to denature and perforate said membrane;  
wherein said stimulus is carried through said supporting member.

45. The method according to claim 44, wherein said membrane is a cell membrane, a cell wall, a biomembrane, or an artificial membrane.

46. The method according to claim 44, wherein said stimulus is selected from the group comprising electromagnetic waves including light, particle rays including radiation, heat, cooling, electricity, magnetism, oscillations including ultrasonic waves, physical contact, chemical substances, living beings including cells, viruses, and any combinations thereof.

47. The method according to claim 46, wherein said stimulus is light and said substance is a photosensitizer.

48. The method according to claim 46, wherein said stimulus is light and said substance is a photocatalyst.

49. The method according to claim 44, wherein said supporting member constitutes a membrane destroying member for perforating the membrane and a stimulus carrying member for carrying the stimulus.

50. The method according to claim 44, wherein said member is a capillary.

51. The method according to claim 49, wherein said member is a capillary.

52. The method according to claim 50, wherein said stimulus is light, said light transmits through the side wall of said capillary as a light guide, and said light is applied to said membrane-denaturing substance from the tip of said capillary.

53. The method according to claim 51, wherein said stimulus is light, said light transmits through the side wall of said capillary as a light guide, and said light is applied to said membrane-denaturing substance from the tip of said capillary.

54. The method according to claim 44, wherein said member is an intracellular sensor.

55. The method according to claim 49, wherein said member is an intracellular sensor.

56. A method of perforating a membrane comprising:

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bringing a membrane-denaturing substance into contact with or close proximity to at least a site of said membrane, said substance inducing a membrane-denaturing reaction by a stimulus; and

providing said stimulus to said substance so as to denature and perforate said membrane; wherein said stimulus is carried through a stimulus-carrying member, and said stimulus-carrying member locally introduces said stimulus to a selected site of said substance.

57. The method according to claim 56, wherein said membrane is a cell membrane, a cell wall, a biomembrane, or an artificial membrane.

58. The method according to claim 56, wherein said stimulus is selected from the group comprising electromagnetic waves including light, particle rays including radiation, heat, cooling, electricity, magnetism, oscillations including ultrasonic waves, physical contact, chemical substances, living beings including cells, viruses, and any combinations thereof.

59. The method according to claim 58, wherein said stimulus is light and said substance is a photosensitizer.

60. The method according to claim 58, wherein said stimulus is light and said substance is a photocatalyst.

61. The method according to claim 56, wherein said stimulus carrying member constitutes a supporting member for supporting the membrane-denaturing substance and a membrane destroying member for perforating the membrane.

62. The method according to claim 56, wherein said member is a capillary.

63. The method according to claim 61, wherein said member is a capillary.

64. The method according to claim 62, wherein said stimulus is light, said light transmits through the side wall of said capillary as a light guide, and said light is applied to said membrane-denaturing substance from the tip of said capillary.

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65. The method according to claim 32, wherein said stimulus is light, said light transmits through the side wall of said capillary as a light guide, and said light is applied to said membrane-denaturing substance from the tip of said capillary.

66. The method according to claim 56, wherein said stimulus is light, and wherein at least one optical fiber extends in the length of said capillary, said fiber is provided inside and/or outside of the capillary, a distal end of said fiber extends to the tip of said capillary so as to apply said light to the substance from the end of said fiber.

67. The method according to claim 56, wherein said member is an intracellular sensor.

68. The method according to claim 61, wherein said member is an intracellular sensor.

69. A microinjection method comprising:  
perforating a membrane using the method as claimed in claim 32; and  
injecting a desired substance into the membrane.

70. The microinjection method according to claim 38, wherein said substance to be injected into said membrane contains a membrane denaturing substance that induces a membrane-denaturing reaction by a stimulus.

71. The microinjection method according to claim 38, wherein said stimulus is light and said membrane-denaturing substance is a photosensitizer.

72. The microinjection method according to claim 38, wherein said stimulus is light and said membrane-denaturing substance is a photocatalyst.

73. The microinjection method according to claim 38, the method comprising filling the capillary with the substance to be injected, penetrating the tip of the capillary into the membrane, and said substance being injected into the membrane through the capillary.

74. A microinjection method comprising:

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perforating a membrane using the method as claimed in claim 44; and  
injecting a desired substance into the membrane.

75. The microinjection method according to claim 43, wherein said substance to be injected into said membrane contains a membrane denaturing substance that induces a membrane-denaturing reaction by a stimulus.

76. The microinjection method according to claim 43, wherein said stimulus is light and said membrane-denaturing substance is a photosensitizer.

77. The microinjection method according to claim 43, wherein said stimulus is light and said membrane-denaturing substance is a photocatalyst.

78. The microinjection method according to claim 43, the method comprising filling the capillary with the substance to be injected, penetrating the tip of the capillary into the membrane, and said substance being injected into the membrane through the capillary.

79. A microinjection method comprising:  
perforating a membrane using the method as claimed in claim 56; and  
injecting a desired substance into the membrane.

80. The microinjection method according to claim 48, wherein said substance to be injected into said membrane contains a membrane denaturing substance that induces a membrane-denaturing reaction by a stimulus.

81. The microinjection method according to claim 48, wherein said stimulus is light and said membrane-denaturing substance is a photosensitizer.

82. The microinjection method according to claim 48, wherein said stimulus is light and said membrane-denaturing substance is a photocatalyst.

83. The microinjection method according to claim 48, the method comprising filling the capillary with the substance to be injected, penetrating the tip of the capillary into the membrane, and said substance being injected into the membrane through the capillary.

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84. An apparatus for perforating a membrane comprising:  
a membrane-destroying member for supporting a membrane-denaturing substance that induces a membrane-denaturing reaction by a stimulus; and  
a stimulus supply source; and  
wherein said stimulus supplied by said supply source is transmitted to said membrane-denaturing substance through said membrane-destroying member, said substance is brought in contact with or close proximity to at least a site of said membrane by said membrane-destroying member, and said stimulus is given to said membrane-denaturing substance so as to perforate said membrane by said membrane-destroying member.

85. The apparatus according to claim 53, said stimulus is selected from the group comprising electromagnetic waves including light, particle rays including radiation, heat, cooling, electricity, magnetism, oscillations including ultrasonic waves, physical contact, chemical substances, living beings including cells, viruses, and any combinations thereof.

86. The apparatus according to claim 54, wherein said stimulus is light and said substance is a photosensitizer.

87. The apparatus according to claim 54, wherein said stimulus is light and said substance is a photocatalyst.

88. The apparatus according to claim 54, wherein said stimulus supply is a light source.

89. The apparatus according to claim 54, wherein said stimulus supply is an electric power source or heat supply, and wherein said membrane-destroying member comprises a light emitting element, said power or heat is converted into the light stimulus by said light emitting element.

90. The apparatus according to claim 53, wherein said membrane-destroying member is a capillary.

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91. The apparatus according to claim 59, wherein said stimulus is light, said light transmits through the sidewall of said capillary as a light guide.

92. The apparatus according to claim 59, wherein said stimulus is light, and wherein at least one optical fiber extends in the length of said capillary, said fiber is provided inside and/or outside of the capillary, a distal end of said fiber extends to the tip of said capillary so as to apply said light to the substance from the end of said fiber.

93. A microinjection apparatus comprising the membrane perforating apparatus as claimed in claim 53.

94. The microinjection apparatus according to claim 62, wherein said membrane-destroying member is a capillary, and filling the capillary with the substance to be injected, penetrating the tip of the capillary into the membrane, and said substance being injected into the membrane through the capillary.

95. The microinjection apparatus according to claim 62, wherein said substance to be injected into said membrane contains a membrane denaturing substance that induces a membrane-denaturing reaction by a stimulus.

96. The microinjection apparatus according to claim 62, wherein said stimulus is light and said membrane-denaturing substance is a photosensitizer.

97. The microinjection apparatus according to claim 62, wherein said substance to be injected into said membrane is selected from the group comprising, nucleic acids, proteins, lipids, membrane structures, micro machines, and magnetic particles.